EMA/336519/2023

European Medicines Agency decision

P/0294/2023

of 11 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for naltrexone (hydrochloride) / bupropion (hydrochloride) (Mysimba), (EMEA-001373-PIP01-12-M05) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0188/2013 issued on 8 August 2013, the decision P/0071/2016 issued on 18 March 2016, the decision P/0332/2016 issued on 2 December 2016, the decision P/0365/2017 issued on 1 December 2017 and the decision P/0390/2021 issued on 8 September 2021,

Having regard to the application submitted by Orexigen Therapeutics Ireland Limited on 10 March 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 June 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for naltrexone (hydrochloride) / bupropion (hydrochloride) (Mysimba), prolonged-release tablet, oral use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Orexigen Therapeutics Ireland Limited, 2nd Floor Palmerston House, Fenian Street, D02 WD37 – Dublin, Ireland.

EMA/PDCO/139641/2023
Amsterdam, 23 June 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001373-PIP01-12-M05

Scope of the application

Active substance(s):

Naltrexone (hydrochloride) / bupropion (hydrochloride)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of obesity

Pharmaceutical form(s):

Prolonged-release tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Orexigen Therapeutics Ireland Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Orexigen Therapeutics Ireland Limited submitted to the European Medicines Agency on 10 March 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0188/2013 issued on 8 August 2013, the decision P/0071/2016 issued on 18 March 2016, the decision P/0332/2016 issued on 2 December 2016, the decision P/0365/2017 issued on 1 December 2017 and the decision P/0390/2021 issued on 8 September 2021.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 24 April 2023.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of obesity

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- prolonged-release tablet, oral use;
- on the grounds that the condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets.

And to:

- the paediatric population from 2 to less than 6 years of age;
- prolonged-release tablet, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of obesity

2.1.1. Indication targeted by the PIP

Treatment of obesity

2.1.2. Subsets of the paediatric population concerned by the paediatric development

From 6 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release tablet

2.1.4. Measures

Area	Description
Quality-related studies	***Study 1*** Development of an age-appropriate oral preparation solid form, for oral use in children from 6 to less than 12 years of age.
Non-clinical studies	***Study 2*** Mice juvenile toxicity study to assess toxicokinetics, CNS parameters, learning, memory, behaviour, and sexual maturation.

	Study 3 Removed in procedure EMEA-001373-PIP01-12-M01.
Clinical studies	***Study 4*** Randomized, open-label, single-dose pharmacokinetic and safety study of naltrexone and bupropion extended-release fixed-dose combination in obese adolescents from 12 to less than 18 years of age. ***Study 5*** Double-blind, randomised, multi-centre, placebo-controlled study to assess safety and efficacy of naltrexone and bupropion as fixed-dose combination, in obese adolescents from 12 to less than 18 years of age. ***Study 6*** Double-blind, randomised, multicentre, placebo-controlled, multiple dose study to assess pharmacokinetics, pharmacodynamics and tolerability of naltrexone and bupropion as fixed-dose combination, in pre-pubertal obese children from 6 to less than 12 years of age. ***Study 7*** Double-blind, randomised, multi-centre, placebo-controlled study to assess safety and efficacy of naltrexone and bupropion as fixed-dose combination, in pre-pubertal obese children from 6 to less than 12 years of age.
Modelling and simulation studies	Not applicable
Other studies	Not applicable
Extrapolation plan	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2033
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of obesity

Authorised indication(s):

- management of weight in adult patients (≥18 years) with an initial Body Mass Index (BMI) of

  ≥ 30 kg/m2 (obese), or

  ≥ 27 kg/m2 to < 30 kg/m2 (overweight) in the presence of one or more weight-related co-morbidities (e.g., type 2 diabetes, dyslipidaemia, or controlled hypertension)

  Treatment with Mysimba should be discontinued after 16 weeks if patients have not lost at least 5% of their initial body weight.

  - Invented name(s): Mysimba
  - Authorised pharmaceutical form(s): Prolonged-release tablet; Blue, biconvex, round tablet of 11.9 mm diameter debossed with "NB-890" on one side
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure